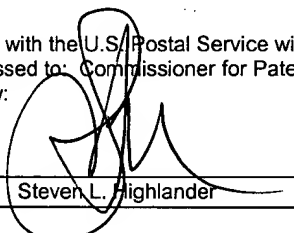




CERTIFICATE OF MAILING
37 C.F.R. §1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-01450, on the date below:

October 6, 2003
Date


Steven L. Highlander

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Sujata KALE and
Michael W. LONG

Serial No.: 09/753,043

Filed: December 27, 2000

For: PROCESS FOR EX VIVO FORMATION
OF MAMMALIAN BONE AND USES
THEREOF

Group Art Unit: 1636

Examiner: Jean C. Witz

Atty. Dkt. No.: UMIC:048US/SLH

DECLARATION OF MICHAEL LONG UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-01450

Dear Sir:

1. I am a citizen of the United States of America, residing at 570 High St., Northville MI 48167.

2. I am the Michael W. Long named as an inventor on the above-captioned patent application. I have been conducting research in the area of bone formation and repair for 18 years. A copy of my *curriculum vitae* is attached.

3. Based on a review of the Office Action mailed on April 4, 2003, it is my understanding that the examiner for above-captioned application has suggested that the bone “nodules” or “globules” described in U.S. Patent 6,152,964 are the same as the bone spheroids of the instant application. However, I believe the examiner to be incorrect in this supposition. The following paragraphs set forth facts that support my position.

4. First, the ‘964 patent requires that the cells be grown on a substrate (Summary; column 2, line 51). The tissue-like aggregates that we grow (referred to as bone cell spheroids) do not require a substrate. Rather, the cells are induced to grow as tissue-like aggregates without a need for structural support.

5. Second, there is a considerable difference in the size of bone cell spheroids and what the ‘964 nodules. FIGS. 1 and 4 in the ‘964 patent are SEM photos. Thus, the material they are describing is, by definition, sub-microscopic. The bone cell spheroids we develop as part of this invention consist of 10,000 to 100,000+ cells. They are thus much larger in size. Likewise the bone synthesized by the cells of the spheroid is larger than the structures apparent in FIGS. 1 and 4 of the ‘964 patent.

6. Third, the ‘964 patent clearly states that ascorbic acid, β -glycerol phosphate, and dexamethasone are “essential for the production of bone-like tissue” (column 4, line 27). These substances are not required for the production of bone cell spheroids, nor are they required for the formation of bone by these cells.

7. Fourth, the ‘964 patent uses undifferentiated bone marrow cells (Summary; column 2, lines 40, 51, 61; column 4, line 21; Claims), and in particular stromal cells (column 2, line 48). The present application specifically uses differentiated bone cells (both preosteoblasts

and osteoblasts). These are specifically isolated from bone fragments in which the bone marrow cells are washed away, and further removed by collagenase treatment.

8. Based on the points set forth above, I believe that it is quite clear that the bone nodules of the '964 patent are distinct from the bone cell spheroids of the present application.

9. I hereby declare that all statements made herein of my knowledge are true and that all statements made herein on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under § 1001 of Title 18 of the U.S. Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date

Michael W. Long, Ph.D.